
JunB protects against myeloid malignancies by limiting hematopoietic stem cell proliferation and differentiation without affecting self-renewal.

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Public Summary:

Research article investigating the mechanisms by which the transcription factor JunB prevents leukemic transformation of blood stem cells.

Scientific Abstract:

Loss of the JunB/AP-1 transcription factor induces a myeloproliferative disease (MPD) arising from the hematopoietic stem cell (HSC) compartment. Here, we show that junB inactivation deregulates the cell-cycle machinery and increases the proliferation of long-term repopulating HSCs (LT-HSCs) without impairing their self-renewal or regenerative potential in vivo. We found that JunB loss destabilizes a complex network of genes and pathways that normally limit myeloid differentiation, leading to impaired responsiveness to both Notch and TGF-beta signaling due in part to transcriptional deregulation of the Hes1 gene. These results demonstrate that LT-HSC proliferation and differentiation are uncoupled from self-renewal and establish some of the mechanisms by which JunB normally limits the production of myeloid progenitors, hence preventing initiation of myeloid malignancies.

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